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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,379	07/06/2001	Hing C. Wong	44470 C1-CPA-C (71758)	4293

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EXAMINER
DECLOUX, AMY M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/900,379	Applicant(s) WONG ET AL.	
	Examiner Amy M. DeCloux	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of the species of Group C as defined in the office action mailed 9-10-02, (Paper No. 6), including the complex of claim 57 wherein the amino acid is Cys, in Paper No. 7, filed 10-15-02, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

The priority date for Claims 51-59 is 1-17-1997, based on parent Application 08/776,084, filed 1-17-1997. Said claims do not receive benefit of parent Applications 08/382,454, filed 2-1-1995, nor 08.283,302, filed 7-29-1994, because said claims do not support a multivalent MHC fusion complex comprising two or more linked MHC fusion complexes. Applicant is invited to point out support for said claims in the two latter mentioned parent applications.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

Rejection under 35 U.S.C 102(e), Patent Application Publication or Patent to Another with Earlier Filing Date, in view of the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 51-53 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,015,884 (Priority to 3-28-1996).

'884 teaches a multivalent MHC fusion complex comprising two or more linked MHC fusion complexes, wherein each MHC fusion complex comprises a MHC Class II molecule that contains a peptide binding groove, a presenting peptide covalently linked to an N terminus of the MHC molecule and effectively positioned in the peptide binding groove, and a linker sequence interposed between the presenting peptide and the MHC molecule, wherein the presenting peptide is encoded by a nucleic acid sequence encoding a leader sequence attached to the

presenting peptide, wherein the MHC fusion complex does not contain the transmembrane and cytoplasmic domains of the MHC molecule and is linked to IgG, IgM or Fab'2, the fusion complex being capable of increasing or decreasing T cell proliferation or development, (see entire patent especially Figure 1C, column 10, lines 32-52, column 12, lines 30-45, column 14, lines 30-60, column 19, lines 20-60, column 20, line 60 through column 21, line 45, column 5, line 35 through column 7, line 6).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 51-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,015,884, in view of US Patent No. 6,083,708, filed 8-11-1995.

6. '884 teaches as above. '884 further teaches that soluble MHC molecules have an intrinsic low avidity for their ligands, and therefore soluble multivalent MHC Class II/peptide complexes were made that have increased avidity for their cognates, and as such will be useful in studying TCR/MHC interactions, lymphocyte tracking, identifying new antigens, and regulating specific immune responses, (see Abstract). '884 also teaches that the recited multivalent MHC fusion complexes can be immobilized on a substrate in order to identify and purify particular T cell subsets that stimulate antigen specific T cell responses (see column 6, lines 9-25). '884 also teaches that amino acid substitutions can be made (column 9, lines 40-43) and that said complexes are made using genetic recombinant techniques (see Example 1).

'884 does not teach multivalent MHC Class II/peptide complexes that are chemically crosslinked together or to a specific particle, such as a dendrimer as recited in claims 54 and 59, nor that the reactive side chains of amino acids such as Cysteine are used to chemically cross link the MHC fusion complexes, as recited in claims 55 and 57, nor that the C terminus of the beta chain is genetically modified to include amino acids with chemically reactive side chains such as Cys as recited in claims 56 and 58.

7. '708 teaches that dendrimer:antibody complexes have been used to form assay reagents by the formation of C-S linkages between a dendrimer derivatized with sulfosuccinimidyl-(4-iodoacetyl) aminobenzoate (sulfo-SIAB) and a Sulfhydryl group on an antibody (see entire patent especially column 1, lines 58-67). '884 also teaches that dendrimer:antibody complexes have been used to overcome some of the problems of polypeptide-polypeptide conjugates including uncontrolled intermolecular conjugation (see column 1, lines 33-67), and include the advantages of being designed to be a precise molecular size, and being uniform over different manufacturing lots (see column 9, lines 1-7), that illustrative reactive moieties may comprise sulfhydral groups of Cysteines, (see column 7, lines 1-8), and that said reactive moieties may also be introduced onto a polypeptide in a separate reaction, (see column 7, line9-10). '708 also teaches that coupling to a dendrimer is carried out such that the original biological activity is retained, (column 7, lines 54-58). '708 also teaches that it is well known to directly covalently couple two different polypeptides to form a conjugated reagent for a diagnostic assay (see entire patent, especially column 1, lines 33-36).

Therefore, one of skill who wanted to use assays to study TCR/MHC interactions, track lymphocytes, and identify new antigens, would have been motivated to have made and used multivalent MHC Class II/peptide complexes in an assay as taught by 884, and to have chemically crosslinked the reactive side chains of amino acids such as Cysteine of said multivalent complexes to a specific particle, such as a dendrimer taught by '708, because '708 teaches that dendrimer:antibody complexes have been used to form assay reagents by the formation of C-S linkages between a dendrimer derivatizzed with sulfosuccinimidyl-(4-iodoacetyl) aminobenzoate (sulfo-SIAB) and a Sulfhydryl group on an antibody (ie Cys), and teaches that dendrimer:antibody complexes have been used to overcome some of the problems of polypeptide-polypeptide conjugates including uncontrolled intermolecular conjugation, and because'708 also teaches that coupling to a dendrimer is carried out such that the original biological activity is retained.

One of skill would also have been motivated to have genetically modified the C terminus of the beta chain to include amino acids with chemically reactive side chains such as Cys, in order to form multivalent complexes, because'884 teaches that multivalent MHC Class II/peptide complexes have increased avidity for their cognates and can be used in assays to study TCR/MHC interactions, track lymphocytes and identify new antigens, and because '708 also teaches that it is well known to directly covalently couple two different polypeptides to form a conjugated reagent for a diagnostic assay and that such reactive moieties may be introduced onto a polypeptide in a separate reaction. '884 also teaches that amino acid substitutions can be made using genetic recombinant techniques as well.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of

ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 8:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305-3014 for regular communications and 703 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, Ph.D.
Patent Examiner,
January 4, 2003

Patrick J. Nolan, Ph.D.
Primary Patent Examiner,
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